Increased Blood Pressure Variability: A Marker of Augmented Sympathetic Vascular Reactivity?

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Several observational studies have reported that increased blood pressure variability is associated with an increased risk of incident cardiovascular disease.[1–3] Interestingly, this finding appears to apply to short-term (ambulatory), midterm (home), and long-term (office) blood pressure variability.[4] Although the prognostic significance of blood pressure variability has been studied extensively, its underlying causes remain mainly unclear. More importantly, the exact mechanisms through which increased variability causes cardiovascular complications are also ambiguous. Some studies have suggested that increased blood pressure variability could be only a surrogate marker of poor adherence to therapy or increased alcohol use, which in turn are causally related to adverse outcomes.[5,6] However, the association between blood pressure variability and cardiovascular disease has persisted in several studies even after controlling for these factors.[4]

Blood pressure is a highly variable hemodynamic phenomenon that is continuously affected by respiration, emotion, exercise, meals, tobacco use, bladder distension, and pain.[7] Temperature also has a major effect on blood pressure as exposure to cold can raise an individual's blood pressure 20 mm Hg through sympathetic activation and peripheral vasoconstriction.[8] Sympathetic overactivity also holds an important key pathophysiological role in heart failure, acute coronary syndromes, and arrhythmias.[9] These prior findings, therefore, raise the possibility that exaggerated sympathetic reactivity could be a major factor behind both increased blood pressure variability and cardiovascular disease.

In their article, Hintsala et al.[10] (this issue) examine the relation of cold exposure, a sympathetic stressor, and home blood pressure variability in a population sample of 75 men aged 55–65 years. Home blood pressure was measured twice in the morning and evening for a period of 7 days. Blood pressure variability was defined as the within-subject standard deviation of daily mean values, whereas high blood pressure variability was defined as variability over median. The participants also underwent a 15-minute cold exposure, and cardiovascular responses were measured before, during, and after the cold exposure. The authors observed that individuals with high blood pressure variability demonstrated greater increases in rate-pressure product (1,850 vs. 930 bpm*mm Hg; $P < 0.01$) and systolic blood pressure (31 vs. 23 mm Hg; $P < 0.01$) in cold conditions compared with those with low blood pressure variability, even after adjusting for confounders. Blood pressure variability was moderately correlated with cold-related rate-pressure product ($r = 0.34$) and systolic blood pressure ($r = 0.38$) responses. The authors' concluded that individuals with higher home blood pressure variability have an exaggerated systolic blood pressure response to stress involving cold exposure.

The authors provide a novel approach to elucidating the factors underlying blood pressure variability.[10] However, the study is still limited by its small sample size, which renders subgroup analyses impossible. Furthermore, the generalizability of the results is reduced due to a study sample, which consisted solely of older white men who were accustomed to living in a colder climate. In addition, the correlation of this finding with other cardiovascular risk factors and prognosis remains unclear. It is also important to remember that the associations observed by Hintsala et al. only apply to home blood pressure variability as it has been previously shown that the correlation between ambulatory, home, and office blood pressure variability is weak.[11] In spite of its limitations, this study nevertheless provides a proof-of-concept for the link between blood pressure variability and exaggerated sympathetic reactivity.

As already noted previously, the physiological factors underlying blood pressure variability and its potential role as an independent cardiovascular risk factor have mainly remained unclear. Prior experimental animal studies have observed that increases in blood pressure variability, without changes in mean blood pressure level, have resulted in left ventricular hypertrophy and aortic vasoconstriction.[12] Furthermore, blood pressure variability is related to raised inflammatory markers in animals and humans.[12,13] It has also been speculated that sudden changes in blood pressure leading to reduced perfusion in the brain could also be

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one of the factors through which increased blood pressure variability predisposes to cardiovascular events.[14]

In addition to a paucity of research on the factors underlying increased cardiovascular risk in the setting of high blood pressure variability, prior studies have also made inconsistent associations between ambulatory blood pressure variability and cardiovascular reactivity.[15–17] Only one previous research letter has reported the association between home blood pressure variability and cold pressor test results in 172 Chinese individuals.[18] The investigators of this study observed that systolic home blood pressure variability was strongly related to blood pressure increases during the cold pressor test. Furthermore, persons with high blood pressure variability demonstrated higher sympathetic activity and reduced parasympathetic activity to an extent.[18] The study by Hintsala et al. expands on these previous results by suggesting that individuals with increased home blood pressure variability have an augmented increase in cardiac work load and blood pressure during a cold response that imitates winter conditions.[10] As a result, stronger evidence now exists of elevated blood pressure variability being an indicator of increased sympathetically mediated vascular reactivity, which, in turn, has been associated with increased risk of incident cardiovascular disease by itself.[19]

The clinical implications of this study are still somewhat unclear and need to be validated using other variability indices and stressors. In any case, the study by Hintsala et al. reminds us that blood pressure variability, whether it be short, mid, or long term, is a complex phenomenon with numerous underlying causes.[10] The results of this study also underscore the importance of evaluating blood pressure variability in patients and identifying potential factors underlying it, such as exaggerated cardiovascular reactivity, excessive alcohol use, diabetes, and prevalent cardiovascular disease.[20] Although additional research on the potential additional underlying factors of blood pressure variability is still needed, more attention should now be focused on conducting clinical trials for (i) defining the optimal treatment methods for increased blood pressure variability and (ii) confirming if a causal relationship exists between blood pressure variability and cardiovascular disease.

DISCLOSURE

The author declared no conflict of interest.

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